

### In the Claims

Please cancel claims 28 – 34 and 38 – 44.

Please amend claims 24 – 27, 35 – 37, and 45 – 67 as follows.

24. (Twice Amended) An isolated Streptococcal pyrogenic exotoxin type C (SPE-C toxin) comprising:

F<sup>2</sup> an amino acid substitution of aspartic acid-12 of SEQ ID NO: 2, tyrosine-15 of SEQ ID NO: 2, tyrosine-17 of SEQ ID NO: 2, histidine-35 of SEQ ID NO: 2, asparagine-38 of SEQ ID NO: 2, or substitution at more than one of these amino acids; and

wherein the mutant is nonlethal compared with a wild type SPE-C toxin.

25. (Amended) The isolated SPE-C toxin of claim 24, wherein the amino acid substitution comprises the substitution of aspartic acid-12 of SEQ ID NO: 2 to alanine, glutamic acid, asparagine, glutamine, lysine, arginine, serine, or threonine; the substitution of tyrosine-15 of SEQ ID NO: 2 to phenylalanine, alanine, glycine, serine, or threonine; the substitution of tyrosine-17 of SEQ ID NO: 2 to phenylalanine, alanine, glycine, glutamic acid, lysine, arginine, aspartic acid, serine, or threonine; the substitution of histidine-35 of SEQ ID NO: 2 to phenylalanine, alanine, glycine, glutamic acid, lysine, arginine, aspartic acid, tyrosine, phenylalanine, serine, or threonine; the substitution of asparagine-38 of SEQ ID NO: 2 to alanine, aspartic acid, glutamic acid, lysine or arginine; or substitution at more than one of these amino acids.

26. (Amended) The isolated SPE-C toxin of claim 25, wherein the amino acid substitution comprises the substitution of aspartic acid-12 of SEQ ID NO: 2 to alanine, the substitution of tyrosine-15 of SEQ ID NO: 2 to alanine or serine, the substitution of tyrosine-17 of SEQ ID NO: 2 to alanine or serine, the substitution of histidine-35 of SEQ ID NO: 2 to alanine, the substitution of asparagine-38 of SEQ ID NO: 2 to alanine, serine, or aspartic acid; or substitution at more than one of these amino acids.

F3  
27. (Amended) The isolated SPE-C toxin of claim 26, wherein the amino acid substitution comprises the substitution of tyrosine-15 of SEQ ID NO: 2 to serine or alanine and of asparagine-38 of SEQ ID NO: 2 to serine, alanine, or aspartic acid; the substitution of tyrosine-17 of SEQ ID NO: 2 to serine or alanine and of asparagine-38 of SEQ ID NO: 2 to serine, alanine, or aspartic acid; or the substitution of tyrosine-15 of SEQ ID NO: 2 to alanine, histidine-35 of SEQ ID NO: 2 to alanine, and asparagine-38 of SEQ ID NO: 2 to aspartic acid.

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F4  
35. (Twice Amended) An isolated SPE-C toxin comprising:  
an amino acid substitution of aspartic acid-12 of SEQ ID NO: 2 to alanine, glutamic acid, asparagine, glutamine, lysine, arginine, serine, or threonine;  
an amino acid substitution of tyrosine-15 of SEQ ID NO: 2 to phenylalanine, alanine, glycine, serine, or threonine;  
an amino acid substitution of tyrosine-17 of SEQ ID NO: 2 to phenylalanine, alanine, glycine, glutamic acid, lysine, arginine, aspartic acid, serine, or threonine;  
an amino acid substitution of histidine-35 of SEQ ID NO: 2 to phenylalanine, alanine, glycine, glutamic acid, lysine, arginine, aspartic acid, tyrosine, phenylalanine, serine, or threonine;  
an amino acid substitution of asparagine-38 of SEQ ID NO: 2 to alanine, aspartic acid, glutamic acid, lysine or arginine; or  
substitution at more than one of these amino acids; and  
wherein the mutant is nonlethal compared with a wild type SPE-C toxin.

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F5  
36. (Amended) The isolated SPE-C toxin of claim 35, wherein the amino acid substitution comprises the substitution of aspartic acid-12 of SEQ ID NO: 2 to alanine, the substitution of tyrosine-15 of SEQ ID NO: 2 to alanine or serine, the substitution of tyrosine-17 of SEQ ID NO: 2 to alanine or serine, the substitution of histidine-35 of SEQ ID NO: 2 to alanine, the substitution of asparagine-38 of SEQ ID NO: 2 to alanine, serine, or aspartic acid; or substitution at more than one of these amino acids.

37. (Amended) The isolated SPE-C toxin of claim 36, wherein the amino acid substitution comprises the substitution of tyrosine-15 of SEQ ID NO: 2 to serine or alanine and

F5 of asparagine-38 of SEQ ID NO: 2 to serine, alanine, or aspartic acid; the substitution of tyrosine-17 of SEQ ID NO: 2 to serine or alanine and of asparagine-38 of SEQ ID NO: 2 to serine, alanine, or aspartic acid; or the substitution of tyrosine-15 of SEQ ID NO: 2 to alanine, histidine-35 of SEQ ID NO: 2 to alanine, and asparagine-38 of SEQ ID NO: 2 to aspartic acid.

45. (Amended) An isolated Streptococcal pyrogenic exotoxin type C (SPE-C toxin) comprising an amino acid substitution at aspartic acid-12 of SEQ ID NO: 2.

46. (Amended) The isolated SPE-C toxin of claim 45, wherein the amino acid substitution comprises alanine for aspartic acid-12 of SEQ ID NO: 2.

F6 47. (Amended) An isolated Streptococcal pyrogenic exotoxin type C (SPE-C toxin) comprising an amino acid substitution at asparagine-38 of SEQ ID NO: 2.

48. (Amended) The isolated SPE-C toxin of claim 47, wherein the amino acid substitution comprises aspartic acid for asparagine-38 of SEQ ID NO: 2.

49. (Amended) An isolated Streptococcal pyrogenic exotoxin type C (SPE-C toxin) comprising an amino acid substitution at tyrosine-15 of SEQ ID NO: 2 and at asparagine-38 of SEQ ID NO: 2.

50. (Amended) The isolated SPE-C toxin of claim 49, wherein the amino acid substitution comprises serine or alanine for tyrosine-15 of SEQ ID NO: 2 and aspartic acid for asparagine-38 of SEQ ID NO: 2.

51. (Amended) The isolated SPE-C toxin of claim 49, wherein the amino acid substitution comprises serine for tyrosine-15 of SEQ ID NO: 2 and serine for asparagine-38 of SEQ ID NO: 2.

52. (Amended) The isolated SPE-C toxin of claim 49, further comprising an amino acid substitution at histidine-35 of SEQ ID NO: 2.

53. (Amended) The isolated SPE-C toxin of claim 52, wherein the amino acid substitution comprises alanine for tyrosine-15 of SEQ ID NO: 2, alanine for histidine-35 of SEQ ID NO: 2, and aspartic acid for asparagine-38 of SEQ ID NO: 2.

54. (Amended) An isolated Streptococcal pyrogenic exotoxin type C (SPE-C toxin) comprising an amino acid substitution at tyrosine-17 of SEQ ID NO: 2 and at asparagine-38 of SEQ ID NO: 2.

55. (Amended) The isolated SPE-C toxin of claim 54, wherein the amino acid substitution comprises serine or alanine for tyrosine-17 of SEQ ID NO: 2 and aspartic acid for asparagine-38 of SEQ ID NO: 2.

56. (Amended) The isolated SPE-C toxin of claim 54, wherein the amino acid substitution comprises serine for tyrosine-17 of SEQ ID NO: 2 and serine for asparagine-38 of SEQ ID NO: 2.

Fl 57. (Amended) An isolated Streptococcal pyrogenic exotoxin type C (SPE-C toxin) comprising an amino acid substitution at tyrosine-15 of SEQ ID NO: 2, at histidine-35 of SEQ ID NO: 2, and at asparagine-38 of SEQ ID NO: 2.

58. (Amended) The isolated SPE-C toxin of claim 45, wherein the amino acid substitution comprises alanine for tyrosine-15 of SEQ ID NO: 2, alanine for histidine-35 of SEQ ID NO: 2, and aspartic acid for asparagine-38 of SEQ ID NO: 2.

59. (Amended) An isolated Streptococcal pyrogenic exotoxin type C (SPE-C toxin) comprising an amino acid substitution at aspartic acid-12 of SEQ ID NO: 2, at tyrosine-15 of SEQ ID NO: 2, at tyrosine-17 of SEQ ID NO: 2, at histidine-35 of SEQ ID NO: 2, at asparagine-38 of SEQ ID NO: 2, or at up to three of these amino acids.

60. (Amended) The isolated SPE-C toxin of claim 59, wherein the amino acid substitution comprises serine or alanine for tyrosine-15 of SEQ ID NO: 2 and aspartic acid for asparagine-38 of SEQ ID NO: 2.

61. (Amended) The isolated SPE-C toxin of claim 59, wherein the amino acid substitution comprises serine or alanine for tyrosine-17 of SEQ ID NO: 2 and aspartic acid for asparagine-38 of SEQ ID NO: 2.

62. (Amended) The isolated SPE-C toxin of claim 59, wherein the amino acid substitution comprises serine for tyrosine-15 of SEQ ID NO: 2 and serine for asparagine-38 of SEQ ID NO: 2.

63. (Amended) The isolated SPE-C toxin of claim 59, wherein the amino acid substitution comprises serine for tyrosine-17 of SEQ ID NO: 2 and serine for asparagine-38 of SEQ ID NO: 2.

64. (Amended) The isolated SPE-C toxin of claim 59, wherein the amino acid substitution comprises alanine for tyrosine-15 of SEQ ID NO: 2.

F-6  
65. (Amended) The isolated SPE-C toxin of claim 59, wherein the amino acid substitution comprises alanine for tyrosine-15 of SEQ ID NO: 2, alanine for histidine-35 of SEQ ID NO: 2, and aspartic acid for asparagine-38 of SEQ ID NO: 2.

66. (Amended) The isolated SPE-C toxin of claim 59, wherein the amino acid substitution comprises aspartic acid for asparagine-38 of SEQ ID NO: 2.

67. (Amended) The isolated SPE-C toxin of claim 59, wherein the amino acid substitution comprises alanine for aspartic acid-12 of SEQ ID NO: 2.

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Please add new claims 68 – 99 as follows.

68. (New) An isolated Streptococcal pyrogenic exotoxin type C (SPE-C toxin) comprising:

an amino acid substitution at aspartic acid-12 of SEQ ID NO: 2,  
wherein the SPE-C toxin has at least 97.5% identity to SEQ ID NO: 2.

69. (New) The SPE-C toxin of claim 68, wherein the amino acid substitution comprises:  
the substitution of aspartic acid-12 to alanine.

70. (New) The SPE-C toxin of claim 68, wherein the percentage identity to SEQ ID NO: 2 is at least 99%.

71. (New) The SPE-C toxin of claim 68, wherein the percentage identity to SEQ ID NO: 2 is 100% at positions other than aspartic acid-12.

72. (New) An isolated Streptococcal pyrogenic exotoxin type C (SPE-C toxin) comprising:

an amino acid substitution at tyrosine-15 of SEQ ID NO: 2,  
wherein the SPE-C toxin has at least 97.5% identity to SEQ ID NO: 2.

73. (New) The SPE-C toxin of claim 72, wherein the amino acid substitution comprises:  
the substitution of tyrosine-15 to serine or alanine.

74. (New) The SPE-C toxin of claim 72, wherein the percentage identity to SEQ ID NO: 2 is at least 99%.

75. (New) The SPE-C toxin of claim 72, wherein the percentage identity to SEQ ID NO: 2 is 100% at positions other than tyrosine-15.

76. (New) An isolated Streptococcal pyrogenic exotoxin type C (SPE-C toxin) comprising:

an amino acid substitution at tyrosine-17 of SEQ ID NO: 2,  
wherein the SPE-C toxin has at least 97.5% identity to SEQ ID NO: 2.

77. (New) The SPE-C toxin of claim 76, wherein the amino acid substitution comprises:

the substitution of tyrosine-17 to serine or alanine.

78. (New) The SPE-C toxin of claim 76, wherein the percentage identity to SEQ ID NO: 2 is at least 99%.

79. (New) The SPE-C toxin of claim 76, wherein the percentage identity to SEQ ID NO: 2 is 100% at positions other than tyrosine-17.

80. (New) An isolated Streptococcal pyrogenic exotoxin type C (SPE-C toxin) comprising:

an amino acid substitution at histidine-35 of SEQ ID NO: 2,  
wherein the SPE-C toxin has at least 97.5% identity to SEQ ID NO: 2.

81. (New) The SPE-C toxin of claim 80, wherein the amino acid substitution comprises:

the substitution of histidine-35 to alanine.

82. (New) The SPE-C toxin of claim 80, wherein the percentage identity to SEQ ID NO: 2 is at least 99%.

83. (New) The SPE-C toxin of claim 80, wherein the percentage identity to SEQ ID NO: 2 is 100% at positions other than histidine-35.

84. (New) An isolated Streptococcal pyrogenic exotoxin type C (SPE-C toxin) comprising:

an amino acid substitution at asparagine-38 of SEQ ID NO: 2,  
wherein the SPE-C toxin has at least 97.5% identity to SEQ ID NO: 2.

85. (New) The SPE-C toxin of claim 84, wherein the amino acid substitution comprises:

the substitution of asparagine-38 to serine, alanine, or aspartic acid.

86. (New) The SPE-C toxin of claim 84, wherein the percentage identity to SEQ ID NO: 2 is at least 99%.

87. (New) The SPE-C toxin of claim 84, wherein the percentage identity to SEQ ID NO: 2 is 100% at positions other than asparagine-38.

88. (New) An isolated Streptococcal pyrogenic exotoxin type C (SPE-C toxin) comprising:  
an amino acid substitution at tyrosine-15 of SEQ ID NO: 2 and asparagine-38 of SEQ ID NO: 2,

wherein the SPE-C toxin has at least 97.5% identity to SEQ ID NO: 2.

89. (New) The SPE-C toxin of claim 88, wherein the amino acid substitution comprises:

the substitution of tyrosine-15 to alanine and asparagine-38 to alanine.

90. (New) The SPE-C toxin of claim 88, wherein the percentage identity to SEQ ID NO: 2 is at least 99%.

91. (New) The SPE-C toxin of claim 88, wherein the percentage identity to SEQ ID NO: 2 is 100% at positions other than tyrosine-15 and asparagine-38.



92. (New) An isolated Streptococcal pyrogenic exotoxin type C (SPE-C toxin) comprising:  
an amino acid substitution at tyrosine-17 of SEQ ID NO: 2 and asparagine-38 of SEQ ID NO: 2,  
wherein the SPE-C toxin has at least 97.5% identity to SEQ ID NO: 2.

93. (New) The SPE-C toxin of claim 92, wherein the amino acid substitution comprises:  
the substitution of tyrosine-17 to alanine and asparagine-38 to alanine.

94. (New) The SPE-C toxin of claim 92, wherein the percentage identity to SEQ ID NO: 2 is at least 99%.

95. (New) The SPE-C toxin of claim 92, wherein the percentage identity to SEQ ID NO: 2 is 100% at positions other than tyrosine-17 and asparagine-38.

96. (New) An isolated Streptococcal pyrogenic exotoxin type C (SPE-C toxin) comprising:  
an amino acid substitution at tyrosine-15 of SEQ ID NO: 2, histidine-35 of SEQ ID NO: 2, and asparagine-38 of SEQ ID NO: 2,  
wherein the SPE-C toxin has at least 97.5% identity to SEQ ID NO: 2.

97. (New) The SPE-C toxin of claim 96, wherein the amino acid substitution comprises:  
the substitution of tyrosine-15 to alanine, histidine-35 to alanine, and asparagine-38 to aspartic acid.

98. (New) The SPE-C toxin of claim 96, wherein the percentage identity to SEQ ID NO: 2 is at least 99%.

99. (New) The SPE-C toxin of claim 96, wherein the percentage identity to SEQ ID NO: 2 is 100% at positions other than tyrosine-15, histidine-35, and asparagine-38.

F9